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Cutaneous Metastasis in Endometrial Cancer and Long Term Survival: A Scoping Review

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ADMINISTRATIVE INFORMATION

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 June 2023 and was last updated on 13 June 2023.

INTRODUCTION

Review question / Objective The cutaneous and soft tissue location of the endometrial cancer metastasis is rare. The aim of the review is to examines the prevalence of cutaneous metastasis, diagnosis and treatment options, and the impact of cutaneous metastasis in endometrial cancer on overall survival.

Background The most prevalent gynecologic cancer is endometrial cancer[1–3].2018 saw 121,600 new cases of cancer diagnosed in Europe, roughly 6.6% of all malignancies found in women. 29,600 cancer-related deaths are predicted to occur each year, accounting for over 3.5% of all cancer-related deaths [4].
Mostly post-menopausal women are affected with endometrial cancer. Endometrial cancer is typically diagnosed in women 60 years of age or older[5–7]. In women under the age of 45, it is unusual[8,9]. Black women are more prone to develop this cancer than White women, and they also have a higher mortality rate from it[10].
Young women 20–29 years old saw a rise in endometrial cancer incidence in the US from 0.6 per 100,000 in 2001 to 1.2 per 100,000 in 2017 (APC 3.6, 95% CI 2.9–4.4), while women 30-39 years old saw an increase from 4.6 per 100,000 in 2001 to 7.5 per 100,000 in 2017 (APC 3.0, 95% CI 2.7–3.3)[11,12].
Rarely, metastasis develop in the brain, bones, liver, adrenal glands, extra-abdominal lymph nodes, and soft tissues[11,13–15]. It is beneficial for imaging specialists and radiologists to be able to identify common and uncommon, early atypical metastatic sites.
Skin metastasis from endometrial cancer are uncommon and rare[16], with a report-ed frequency of 0.8%. After the discovery of cutaneous metastasis, the mean life expectancy for endometrial cancer patients is reported to be between 4 and 12 months, which is associated with a dismal prognosis. .The amount of time

between diagnosis and the onset of cutaneous recurrences is a factor that affects survival [17–19]. At the time of diagnosis, the majority of patients (77%) have an early-stage disease with a good overall survival(OS). When the disease has spread, the 5-year survival rate drops from 95% for localized disease to under 20%[20]. Early detection and treatment im-prove patient prognosis.
In this research study we wanted to establish a theory regarding long overall survival despite huge cutaneous metastasis. Our scoping review aim is to examine the prevalence of cutaneous metastasis, diagnosis and treatment options, and impact of cutaneous metastasis in endometrial cancer on overall survival.

Rationale Our goal in doing this study was to develop a theory underlying prolonged overall life in spite of significant cutaneous metastasis. Examining the frequency of cutaneous meta-stasis, available diagnoses and therapies, and survival times are the main objectives of this scoping review.

METHODS

Strategy of data synthesis We performed a systematic search of the current literature of Pubmed and Pubmed Central. For there search we used the following search keywords: endometrial carcinoma, endometrial adenocarcinoma, metastasis, longterm survival, 5-years survival, soft tissue metastasis, cutaneous metastasis, 5-years overall survival. We combined these keywords with the Boolean operator "AND" as following: endometrial carcinoma metastasis AND longterm survival, endometrial carcinoma AND metastasis AND 5 years survival, endometrial carcinoma AND soft tissue metastasis, endometrial carcinoma AND cutaneous metastasis, endometrial carcinoma AND 5-year overall survival, endometrial adenocar-cinoma AND soft tissue metastasis, endometrial adenocarcinoma AND cutaneous meta-stasis, endometrial adenocarcinoma AND 5-year overall survival and endometrial adenocarcinoma AND longterm survival.

Eligibility criteria To narrow down our research, we limited the study selection on studies published between 2003 and 2023. Additionally, we used the following filters: case report, comparative study, meta-analysis, review, systematic review, humans, English, German, 2003-2023.

Source of evidence screening and selection The studies were examined by two separate researchers (Nienhaus and Rajaku-lendran), who screened the articles and excluded the duplicates in the first stage. Next, abstracts of all potentially relevant papers were individually assessed for suitable for our review.
We examined the following topics: the time from the initial diagnosis to cutaneous metastasis, the initial operative therapy, the localization of the metastasis, the FIGO stage at the initial diagnosis of the endometrial carcinoma, the therapy of the initial diagnosis, therapy of the metastatic disease and the time from diagnosis of the cutaneous metastasis to death. For this, we created different table stop resent our results more clearly.

Data management We found eight case report studies for cutaneous metastasis from endometrial cancer. There were patients between 52 and 73 years old in the cohort. The histological type of the metastasis was in six cases endometroid adenocarcinoma, in one case carcinosarcoma and in one case leiomyosacoma. The time from the diagnosis of endometrial cancer to the apparence of cutaneous metastasis was between 2 months and 3 years.
The localisation of cutaneous metastasis may vary. In two sudies there were shown metastasis on the skull, two studies showed metastasis on the vulva . Metastasis were also located on the trunk, breasts, flank and lower leg. The initial operation performed for endometrial cancer depended on the FIGO Stage, with total abdominal hysterectomy, bilateral salpingo-oophorectomy with or without pelvic and paraaortallyphnodectomy. Some patients had only a lymphnodes sampling. When lypmhadenctomy was performed, in most cases there were metastasis in the lymphnodes shown.We could see that after the apparence of cutaneous metastasis the overall survival rate is poor, between 2 weeks to 14 months. The therapy produced no signifficant change on the overall survival rate. Chemotherapy was performed in four studies and radiotherapy in one case. Hormon therapy was performed in 2 cases and in one case no therapy was performed due to poor general condition. The apparence of cutaneous metastasis was never the only sign of metastasis. In most cases there were also signs of pulmonary, intraabdominal, lymphnodes metastasis and pleural effusion.

Reporting results / Analysis of the evidence Although early-stage disease limited to the uterus is found in the majority of women with EC, a sizable portion of cases also have metastatic disease.[27]
Our Patient was diagnosed with an advanced stage of disease in the lymphatic nodes and had an relapse after 10 years of progression free survival. This is an unusual finding with a big

metastasis of the soft tissue from the chest wall including bone distruction and cutaneous metastasis.

Presentation of the results Endometrial primary malignancy can metastasize most commonly to the vagina or perineum. Rarely, these tumors metastasize to soft tissues or cutaneously. In most cases the overall survival rate is poor, between months and only few years.
Skin metastasis from endometrial cancer is extremely uncommon, despite the fact that endometrial cancer one of the most common cancers in women is. Subcutaneous nodules are a sign of broad spreading and a sign of impending death, showing that these patients have a terrible prognosis.
In our case, we see a rare long survival, with poor symptoms beeing unusual to the big and severe metastasis of the chest wall with invasion of the thorax. At the first diagno-sis of endometrial cancer, the patient presented a metastasis of the navel and metastatic lymph nodes. It is the only case found in the literature review of more than 10 years of survival after having cutaneous metastasis.
The examination of the skin in patients with diagnosis of endometrial cancer even after having received local or systemic treatment is crucial. Nowadays, we have new therapy options in locally or metastatic endometrial cancer, in the form of immune thera-py. So, a histological probe of metastasis is needed when we diagnose it.

Language restriction English and German.

Country(ies) involved Germany and Romania.

Keywords endometrial carcinoma, metastasis; long term survival; soft tissue metastasis; cutaneous metas-tasis; 5-yearoverall survival.

Contributions of each author

Author 1 - Alexandra Nienhaus - designed the study, initiated the collaborations, cleaned and analysed the data, created the figures and tables, interpreted the results, and drafted and revised the manuscript with others. Also contributed to the literature overview, and intellectual inputs interpreted the results and edited the manuscript.contributed to the study concept and design instructed.
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